Ficus exasperata (Vahl) plant: A brief review of its phytochemical properties and pharmacology

ABSTRACT

Background:

In traditional medicine, different parts of *Ficus exasperata* Vahl. (Moraceae) are used as antidiabetic, anticonvulsant, antiinflammatory, antimicrobial, hypolipidemic, antioxidant, antiulcer, anxiolytic and hypotensive, antiarthritic, diuretic, wound healing, antiparasitic, vermifuge, abortifacient, ecbolics and for treating hemorrhoids and venereal diseases. The plant parts are also used as animal fodder.

Aim:

The aim of the review was to……

METHODOLOGY

A documentary search was carried out using data from Google Scholar, PubMed, Elsevier, ScienceDirect, Sciencedomain and Scifinder to examine published scientific reports, ethnobotanical and ethnopharmacological books on its phytochemical constituents and pharmacological properties.

Results:

The medicinal qualities of *Ficus thonningii* are attributed to a variety of bioactive substances, such as Tannins, Flavonoids, Saponins, Phlobatannins, Steroids, alkaloids, anthraquinones and essential oils have also been identified. The bark, leaves, fruits and latex of *F. exasperata* are considered to be very effective in diabetes, skin diseases, ulcers, dysentery, diarrhea, stomachache, hemorrhoids and as carminative, astringent, anti-inflammatory, anti-oxidant and anti-cancer agents in both in vitro and in vivo pharmacological investigations.

Conclusion:

The findings of this study would be useful in developing a monograph for the plant. The data collected can also be used to formulate TAMs (Traditional Improved Medicines) in order to propose safe and effective medicines.

Keywords: Traditional uses, phytochemistry, pharmacology, *Ficus exasperata (Vahl)* .

1. INTRODUCTION

Plants have always been part of human culture and are wide spread in Africa. During the last decades, herbs have been used in culinary and traditional therapeutic practices for the treatment of different ailments. The nutritional and medicinal properties of the

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plant may be inter-linked through the phytochemicals presents in these plants. The natural composition of medicinal plants may act as new alternative in treating various emerging infectious diseases [1,2,3]. Herbal medicine as a form of complementary and alternative medicine in the treatment of diseases is becoming increasingly popular in both developing and developed countries [4,5]. Phytomedicine has demonstrated its contribution to the reduction of excessive mortality, morbidity and disability due to diseases such as HIV/AIDS, malaria, tuberculosis, sickle cell anaemia, diabetes, mental disorders [6] and microbial infections [7].

The genus Ficus belongs to the family moraceae. Ficus comprises about 1000 species distributed to the tropics and temperate regions [8]. The genus is economically important most especially because of their medicinal values occasioned by the richness in secondary metabolites such as flavonoids stilbenes, triterpenoids and xanthones [9]. Preparation of the combination of parts such as leaves, barks, latex and fruits proved effective for the treatment of haemorrhoids, diabetes, stomachache, skin diseases, diarrhoea, dysentery and ulcers [10]. In addition, the preparation is equally very useful as anti-cancer agents, carminative, anti-oxidant, anti-inflammatory and astringent. In another sets of studies [11,12] *Ficus* species were used for the treatment of pile, tuberculosis, ulcer, hypertension, asthma, diarrhoea, diabetes, stomach ache and constipation in in southwestern Nigeria.

The leaf extract has been used ethno-medicinally to treat high blood pressure, rheumatism, arthritis, intestinal pains and colics, epilepsy, bleeding and wounds [13]. Some biological studies indicate that leaves of *F. exasperata* exhibit anti-ulcer, hypotensive, hypoglycemic, hypolipidemic, anti inflammatory, anxiolytic, oxytocin inhibiting, anticonvulsant, antinociceptive, antipyretic, anti microbial, anti candidal, insecticidal, pesticidal activities, antiarthritic and antioxidant [14, 15, 16 ,17 ,18,19,20]. The leaves, stem bark and roots are reported to contain certain phytochemicals such as steroids, flavonoids, phlobatannins, tannins and saponins [21,22] alkaloids, cardiac glycosides,[23] and a new unnamed acylglucosylsterol [24] ; unusual fatty acid from the leaves.

However, recent toxicity studies in rats involving crude aqueous and ethanol extract of the leaves have indicated potential hepatic and renal toxicity as reflected by significantly increased serum transaminases and bilirubin [25, 26].

The present review is aimed to provide a comprehensive account of its traditional uses, phytochemistry, pharmacological activity and toxicity in view of the many recent findings on this plant. This review serves as a collective reference for the researchers to take-up intensive toxicological evaluation and characterization of the toxicants present in *F. exasperata* extracts for its optimum therapeutic use.

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2. Botanical description, habitat and distribution

Ficus exasperata is widely distributed in tropical Africa, from Senegal to Ethiopia and Djibouti, and southwards to Mozambique and Angola. It is also found in Yemen, India and Sri Lanka [27].

Ficus exasperata tree is known as a "sandpaper tree" because of its distichous, alternating, ovate to elliptic, subcoriaceous to coriaceous, apex that is short and acuminate, base that is acute to obtuse, and upper surface that is scabrous and extremely rough. Lateral veins: three to five pairs, with the basal pair branching out to the margin at or above the lamina's middle. Stipules are caducous, strigose, and 0.2–

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0.5 m long, while the petiole is 0.5–4 cm long [27]. In the leaf axils, figs can be found alone or in pairs; they are rarely found on older wood. Fresh figs are subglobose, 1-3cm, hispidulous, and have a peduncle. The basal bracts are 0.5-1 m long and 1 mm long, and they are scattered on the peduncle [27]. Gummy sap emerges from the smooth, greyish cream bark, which has brown streaks. The fruits occur in pairs or solitary in the leaf axils, just below the leaves. The unripe fruit is green in colour, and about 8–15 mm in diameter. The fruits are orange in colour when ripe. It can also survive in cleared areas between 0 and 2000 meters above sea level.

Figures 1, 2 and 3 show the tree, its leaves and fruits.

Fig 1. *F. exasperata* tree

Fig 2. *F. exasperata* leaves

Fig 3. *F. exasperata* fruits

3. Taxonomy, common names and synonyms [28,29]

3.1. Taxonomy

Kingdom: Plantae

Subkingdom: Viridaeplantae

Phylum: Tracheophyta

Subphylum: Euphyllophytina

Infraphylum: Radiatopses

Class: Magnoliopsida

Subclass: Dilleniidae

Superorder: Urticanae

Order: Urticales

Family: Moraceae

Tribe: Ficeae

Genus: *Ficus*

Specific epithet: *exasperata*– Vahl.

Botanical name: *Ficus exasperata* Vahl.

3.2. Common names

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- French: papier de verre
- English: Sandpaper
- Diola: bugnia, busas ,buwés
- Peulh :gnégne
- Mandingue :kotoro lé ,kuturu lé

3.3. Synonyms

Ficus asperrima Roxb., *Ficus punctifera* Warb., *Ficus scabra* Willd., *Ficus silicea* Sim.

4. Traditional use

4.1. Leaves

Traditionally, different parts of the *F. exasperata* are used for the following household, industrial and medicinal purposes. The small thorny leaves are used to polish furniture and slates made of wood [30] In some regions of Africa, the rural population also uses the leaves' scabrous surface as an exploring tool [31] The leaves are a useful source of nutrition for animal keepers. *F. exasperata* leaves are highly valued for their ability to treat a wide range of illnesses. A infusion of the leaves is used to treat gastrointestinal issues in Guinea conacry [32] Haemostatic ophthalmia, coughs, haemorrhoids, anxiety disorders, epilepsy, high blood pressure, rheumatism, arthritis, cancer, intestinal aches, colics, bleeding, and wounds are among the conditions that the leaves are used to cure [13–33]. In some regions of Cameroon, leaves are used for treating haemorrhoids [34], and the leaves' water extract is used orally to treat diarrhoea [35].

For four days, people with diarrhoea are given a glass of extract that is created by macerating a handful of contused leaves in one litre of water [35]. The young leaves are commonly used as an anti-ulcer treatment in Nigeria. It is said that a few leaves that are chewed and swallowed three times over the course of four to eight weeks can completely treat ulcers [14]. The infusion is administered orally as an abortifacient, while the dried leaf powder is used to treat vaginal rash in Sierra Leone [36]. To induce contractions during childbirth, a water extract of the dried leaves is applied topically and ingested orally [37]. In a medication combination for eruptive skin disease, dried leaf is used externally [36]. In Gambia, when someone has chest trouble, they boil the leaves in water and inhale in the steam.

4.2. Roots

Additionally, the roots are used to treat venereal illnesses, asthma, and dyspnoea [38]. In Tanzania, fresh leaves are rubbed to relieve tonsillitis and throat inflammation, while a decoction produced from dried root bark is taken orally to cure asthma. It is also used to treat common eye conditions.

In addition to being used as an ascaricide, dried blossoms are consumed to ease sore throats [39]. To treat eczema, *F. exasperata* root paste and bark mashed with *Croton roxburghii* root in coconut milk are administered externally [40]. In Senegal (Lower Casamance), the decoction of leaves and roots is recognised for its powerful diuretic properties.

The active components of *F. exasperata* are unknown, despite the fact that several extracts of its various portions have been reported to have a variety of pharmacological actions. Steroids, flavonoids, phlobatannins, tannins, and saponins have been reported to be found in the leaves, stem bark, and roots, although [15,22]. Ogunleye

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et al., [23] found that the aqueous extract of leaves included cardiac glycosides, alkaloids, tannins, flavonoids, and saponins.

For the greatest potential therapeutic use, it is crucial to characterise the different *F. exasperata* extracts. Therefore, there is potential for carrying out thorough studies on the phytochemical components of *F. exasperata.*

5. Phytochemical components

Phytochemical analysis of the leaf, stem bark and root of *F. exasperata* shows the presence of tannins, flavonoids, saponins, phlobatannins and steroids, and an absence of alkaloids and anthraquinones [22].

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- Flavonoid glycosides are reported for the first time in this plant species. These are apigenin C-8 glucoside (1), isoquercitrin-6-O-4- hydroxybenzoate (2) and quercetin-3-O-β-rhamnoside (3) [41]. The compounds are shown in Figure 4.

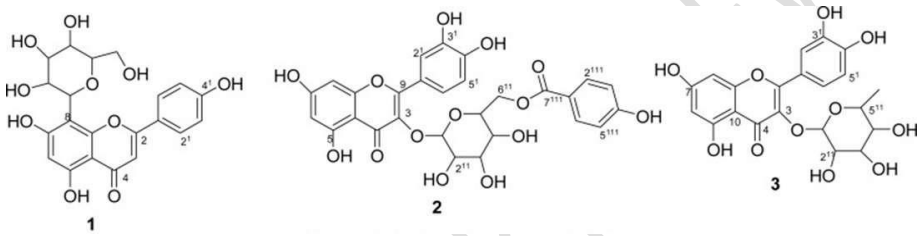

Fig 4. Flavonoid glycoside structure

Chromatographic analysis of the active chloroform fraction of the stem bark yielded Bergapten (1), oxypeucedanine hydrate (2) and β sitosterol- 3-O-β-D-glucopyranoside (3).These compounds are shown in Figure 5 [42].

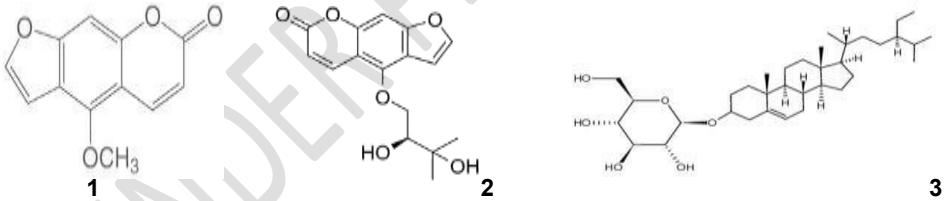

Fig 5. Structure of Bergapten (1), oxypeucedanine hydrate (2) and β sitosterol-3-O-β-D-glucopyranoside (3).

The proximate analysis showed that the fruit contain valuable nutrients: crude protein, crude fibre, ash, crude fat, moisture content and carbohydrate. The analysis of the fruit's minerals revealed the presence of potassium, calcium, iron, titanium, manganese, copper, chromium and nickel. The fatty acids profile showed that the fruit oil contains higher proportion of unsaturated fatty acids, linoleic acid and oleic acid. The major saturated fatty acids detected include stearic acid and palmitic acid [43]. Ethyl acetate extract of *Ficus exasperata* bark contains a triterpenoid: α-amyrin acetate. Fig 6 shows structure of α-amyrin acetate

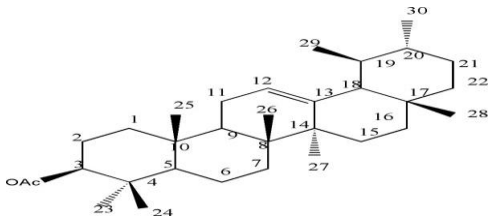

Fig 6. Structure of α-amyrin acetate

The chemical composition of the essential oil of *F. exasperata* leaves is as follows [44]:

α-Pinene (2,2%),p-Cymene (15,4%),1, 8-cineole (13,8%),β-Caryophyllene (3,8%),α-Ionone (2,9%),Neryl acetone (4,2%),β-Ionone (7,5%),Caryophyllene oxide (5,4%),6,10,14-Triméthyl-2-pentadécanone (7.0%),9-Octadecenoic acid (2.9%),Cyclooctasulfur^{+} (6.3%) and (E)-Phytol (13.7%).

All the other reported compounds were identified at concentrations above 2%.

6. Pharmacological propreties

6.1. Antiarthritic activity

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Abotsi *et al.,* (2010) [45] evaluated the activity of the hydroethanol extract of *F. exasperata* leaves against Freund's adjuvant-induced arthritis in rats. After oral administration of the extract (30-300mg /kg) for 29 days, there was a significant dose-dependent reduction in arthritic oedema in the ipsilateral paws of rats to an extent of 34% and also significantly prevented the spread of oedema from ipsilateral to the contralateral paws indicating inhibition of systemic spread. The extract also suppressed pathological changes in the bone and inhibited the radiological index by 95%, compared to untreated rats, indicating anti-arthritic potential [8].

6.2. Antiinflammatory activity

The anti-inflammatory activity of the extract was assessed using the carrageenan-induced foot oedema model in seven-day-old chicks. Hydroalcoholic stem bark extract (30-300 mg/kg) dose-dependently inhibited carrageenan-induced foot oedema with a maximum inhibition of 68.57 ± 3.342 % at 300 mg/kg), which was comparable to that of diclofenac (71. 56 ± 3.43 % at 100 mg/kg) and dexamethasone (74.53 ± 5.21 % at 3 mg/kg). The anti-inflammatory activity is due to secondary metabolites present in the bark. Bergapten, oxypeucedanine hydrate and β sitosterol- 3-O-β-D-glucopyranoside exhibit anti-inflammatory, antioxidant activities and thus contribute substantially to the bioactivities of F. exasperata stem bark [42]. It is reported that α-amyrin acetate possesses effects against erectile dysfunction, anti-inflammatory properties, analgesic properties, *Streptococcus* growth inhibitory effect, antihyperglycaemic, larvicidal, cytotoxic and antispasmodic, leukaemic cell DNA apoptosis, antihepatoxic and antioxidant [46].

6.3. Anticonvulsant activity

Woode *et al.,* [18] evaluated the anticonvulsant properties of *F. exasperata* leaves hydroethanol extract (30:70v/v) against seizures in mice induced by picrotoxin, pentylenetetrazole, or maximum electroshock.

The extract (30-300g kg^{-1}, p.o.) decreased the length of maximal electroshock-induced tonic hind limb extension and significantly delayed the onset and duration of convulsions resulting from pentylenetetrazole and picrotoxin. The extract significantly decreased the time spent on the rotating rod. The researchers came to the conclusion

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that *F. exasperata extract* had strong anticonvulsant properties in mice, confirming its application in African traditional medicine.

6.4. Antihepatoprotective and Antioxidant activities

Hydro-ethanol extract (30:70v/v) of F. exasperata leaves showed significant dose dependent DPPH radical scavenging activity comparable to that of n-propyl gallate with an IC_{50} value of 0.499g mL^{-1}. Further, the extract also exhibited significant dose dependent inhibition of lipid peroxidation in rat brain homogenates in vitro as reflected by significantly lower thiobarbituric acid-reactive substances with an IC_{50} value of 1.283g mL^{-1}. The extract also showed significant reducing capacity in potassium ferricyanide system[45]. The ethanol extract of *F. exasperata* leaves showed that incubation of the tissue homogenates with the pro-oxidants caused significant ($P<0.05$) increase in levels of thiobarbituric acid reactive substances (TBARS), while administration of the extracts provided a significant protection to TBARS levels in the tissues, indicating a protective inhibitory potentials on the pro-oxidants [47]. These effects may be due to the high antioxidant activity of flavonoids, tannins, steroids and saponins isolated from the plant extract, which may protect liver membranes from damage [48].

6.5. Hypoglycaemic and hypolipidaemic activities

Adewole *et al.,* (2011) [16] evaluated the hypoglycaemic potential of *F. exasperata* leaf extract in streptozotocin-induced diabetic rats (spontaneously hypertensive and obese Zucker rats). After 4 weeks of treatment with the extract (100mg kg-1), there was a significant reduction in hyperglycaemia, polyuria and hyperlipidaemia and an increase in serum insulin levels. The authors concluded that *F. exasperata* leaf extract possesses hypoglycaemic and hypolipidaemic properties that support its folkloric and ethnomedical use in diabetes management [8].

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6.6. Antimicrobial activity

With minimum inhibitory concentrations (MIC) of 300 and 700 mg mL^{-1} for *Escherichia coli* and *Staphylococcus albus*, respectively, the ethanol extract of *F. exasperata* leaves showed moderate antibacterial activity against these two bacteria, although the MIC for *S. albus* was 700 mg mL^{-1}.

On the other hand, the crude plant extract revealed strong antibacterial effects when combined with the protein synthesis inhibitors.[18]. The methanol leaf extract inhibited the growth of *P. aeruginosa, S. typhi, S. aureus,* and *E. coli* with MIC values of 75.0, 1.0, 5 and 1.25mg mL-1 respectively. The stem bark methanol extract inhibited the growth of *P. aeruginosa* and *S. Typhi* with MIC values of 75 and 1.25g mL-1, respectively. Similarly, the methanol extract of the root inhibited the growth of *P. aeruginosa, S. typhi, S. aureus, E. coli* and *Vibrio cholerae* with MIC values of 50, 5.0, 1.5, 1.25 and 1.25mg mL-1, respectively. In another study, methanol extract at 400 mg/ml compared favorably well with ciprofloxacin and exhibited the highest antibacterial efficacy on E. coli (22.13 ± 0.25^{h}) while chloroform extract showed the least. Purified extracts recorded higher efficacy compared to the crude extracts. The

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highest activity was recorded for methanol extract at 200 mg/ml against K. pneumoniae (32.98 ± 0.82^{d}) while the least was aqueous extract against *E. coli* (17.96 ± 0.33^{a})[49].

6.7. Antiulcer activity

The *F. exasperata* extract showed a significant, dose dependent decrease in ulcer index and delayed the small intestinal transit in mice, an effect considered beneficial in ulcer patients. Intestinal transit time was inhibited by the reduction in the charcoal meal transit was dose dependent and a maximum inhibition of 81% was observed at the dose of 400mg kg-1, thus significantly delaying the gastric emptying. The extract also increased the pH and reduced the volume and total acidity of the gastric secretion [50].

6.8. Toxicity activities

Several toxicity studies have been conducted on various extracts of *F. exasperata* leaves. Few have shown potential toxic effects, while others have rendered the extracts to be relatively safe. A summary of the toxicity studies is presented here.

Oral administration of the ethanol leaf extract (50, 100 and 150mg kg^{-1}) for 8weeks significantly increased the levels of aspartate aminotransferase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), total bilirubin and conjugated bilirubin in Wistar rats. Similarly, oral administration of the ethanol extract (50, 200 and 500mg kg-1) significantly increased body weights, mean relative kidney weights, serum urea and sodium concentrations in a dose dependent manner in albino rats suggesting that higher doses of the extract could affect kidney function [51]

In an acute toxicity study, oral administration of single dose of the aqueous leaf extract (2.5, 5, 10, and 20g kg^{-1}) did not produce any mortality and changes in behavior andany other physiological activity in mice over 24h. the extract did not affect the body temperature, body weights, blood cell counts and hemoglobin. The LD50 value could not be determined in oral administration route. In another study, hydroethanol extract (20:80v/v) of leaves from *F. exasperata* showed no toxic effects in brine shrimp lethality test, inhibition of telomerase activity, and induction of chromosomal aberrations *in vivo* in rat lymphocytes rendering it relatively safe for possible human consumption [51]. The biochemical findings were substantiated by the histopathological studies which indicated that high doses of the ethanol leaf extract could lead to toxic injury in the kidneys which might interfere with renal tubular function and induce renal failure [25,26].

Although, the plant is traditionally used for the management of various diseases and disorders, its continued usage for medicinal purposes might do more harm than good if toxicity exists. Therefore, in-depth toxicological evaluation is needed to through more light on the safety of *F. exasperata*.

7. CONCLUSION

It is clear from the literature that various portions of *Ficus exasperata* have a wealth of medicinal benefits. To justify the use of this plant or its constituents in traditional remedies, however, more scientific research using contemporary methods is needed.

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To reduce the demand and competition for foods high in protein, research is also necessary to assess this plant's potential for use as animal feed. This review is anticipated to be very helpful in the isolation of new bioactive chemicals and the development of new medications from *F. exasperate*. The safe usage of this plant or its parts must also be assessed by in vitro and in vivo research.

8. DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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